

Attorney Docket No.: UT-0006  
Inventors: Rao et al.  
Serial No.: 09/109,858  
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**I. Rejection of Claims 12, 15, 16, 21, 23, 26-33 and 59 under 35**

**U.S.C. § 112, first paragraph**

Claims 12, 15, 16, 21, 23, 24, 26-33 and 59 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner suggests that the specification does not provide sufficient guidance for obtaining an embryonic neural adhesion molecule antibody which can be used in the claimed methods for isolating a population of cells expressing embryonic neural cell adhesion molecules. Further, the Examiner suggests that it is not readily apparent that this antibody is readily available to the public.

The Examiner has indicated that the requirements of 35 U.S.C. § 112, first paragraph would be satisfied by a deposit of the strains.

In accordance with MPEP § 2404 and 37 C.F.R. § 1.802(b), however, a biological material need not be deposited, inter alia, if it is known and readily available to the public or can be made or isolated without undue experimentation. A deposit is only

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required when access is not otherwise available absence the deposit.

Accordingly, in an earnest effort to advance the prosecution of this case and in accordance with MPEP § 2404.01, Applicants are providing herewith evidence that the embryonic neural adhesion molecule antibody specific for the sialylated form of NCAM is commercially available through the Developmental Studies Hybridoma Bank at the University of Iowa. This commercial source for the antibody is also taught in the application in Example 1 at page 25. Thus, since the public clearly has access to an embryonic neural adhesion molecule antibody for use in the claimed methods of the present application, additional deposit of this antibody is not required to meet the enablement requirements of 35 U.S.C. § 112, first paragraph.

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested in light of Applicants submission of evidence of commercial availability of the embryonic neural adhesion molecule antibody.

**II. Rejection of Claims 12, 15, 16, 21, 23, 24, 26-33, 44 and 59 under 35 U.S.C. § 112, second paragraph**

Claims 12, 15, 16, 21, 23, 24, 26-33, 44 and 59 have been rejected under 35 U.S.C. § 112, second paragraph, as being

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indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claim 12 is suggested to be vague and indefinite for the phrase NEP medium as it is unclear what the components are in said medium. Applicants respectfully disagree.

MPEP § 2173.02 is quite clear; definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) the content of the particular application disclosure;
- (B) the teachings of the prior art; and
- (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

The components of NEP medium are set forth in detail in the application disclosure at page 22, lines 4-12. Thus, contrary to the Examiner's suggestion, what is meant by this phrase is quite clear when read in light of the teachings of this application.

Claim 12 is also suggested to be unclear in step (c) as to whether the cells are replated in the presence of a medium and in step (d) as to how the subpopulation of cells is purified. With respect to step (c) in an earnest effort to advance the prosecution of this case, Applicants have amended the claim to clarify that the cells are plated on laminin coated plates in NEP medium in the

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absence of CEE. Support for this amendment can be found at page 22 of the specification and throughout the Examples. With respect to step (d) the claims have been amended to clarify that the procedures are performed with an embryonic neural cell adhesion molecule antibody. Support for this amendment can be found throughout the specification and in particular in Example 3.

Claims 21, 23, 24 and 59 are also suggested to be vague and indefinite with respect to how the cells are purified. Accordingly, these claim have also been amended in accordance with the Examiner's suggestion to clarify that an embryonic neural cell adhesion molecule antibody is used.

Claim 28 is suggested to be vague and indefinite with respect to the source of the neuron-restricted precursor cells. Accordingly, in an earnest effort to advance the prosecution, Applicants have amended claim 28 to clarify the source of the neuron-restricted precursor cells as rodent or human cells. Support for this amendment can be found throughout the specification and in pending claims 12, 21 and 59. Applicants respectfully disagree with the Examiner that specific steps of the methods by which these cells are obtained are required for clarity of the claim since several methods are set forth in detail in the

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application. Thus, the claims, when read in light of the specification as required by MPEP 2173.02, are clear.

Withdrawal of these rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested in light of the amendments to the claims and the above arguments.

### **III. Provisional Obviousness-type Double Patenting Rejection**

Claims 26 and 27 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 32 of copending Application No. 08/909,435. The Examiner has acknowledged that the conflicting claims are not identical but suggest that they are not patentably distinct from each other because the population of neuron restricted precursor cells of the instant invention is encompassed in the claimed pure population of rodent or human neuron restricted precursor cells of copending Application No. 08/909,435.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicant is submitting herewith a Terminal Disclaimer with respect to copending U.S. Patent Application Serial No. 08/909,435 and the requisite fee for the Terminal Disclaimer.

Withdrawal of this rejection is therefore respectfully requested.

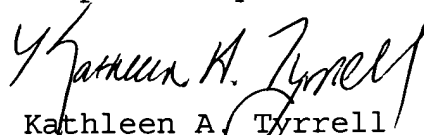
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#### IV. Conclusion

Applicants that this submission overcomes all pending rejections in this case and comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Please amend the claims as follows:

12. (amended) A method of isolating a pure population of rodent or human CNS neuron-restricted precursor cells comprising the steps of:

(a) isolating a population of rodent or human multipotent CNS stem cells which generate both neurons and glia;

(b) incubating the multipotent CNS stem cells in NEP medium;

(c) replating the multipotent CNS stem cells on laminin in NEP medium in the absence of chick embryo extract to induce cell differentiation;

(d) purifying from the differentiating cells a subpopulation of cells expressing embryonic neural cell adhesion molecules via a procedure selected from the group consisting of specific antibody capture, fluorescence activated cell sorting, and magnetic bead capture, wherein said procedure uses an embryonic neural cell adhesion molecule antibody; and

(e) incubating the purified subpopulation of cells in a FGF-containing medium configured for supporting adherent growth thereof to obtain an isolated, purified population of rodent or human CNS neuron-restricted precursor cells, wherein said neuron-

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restricted precursor cells differentiate into CNS neuronal cells upon replacement of adherent growth supporting medium with retinoic acid containing medium and fail to proliferate or differentiate in astrocyte-promoting medium containing FGF and 10% fetal calf serum.

21. (amended) A method of isolating a pure population of rodent or human CNS neuron-restricted precursor cells comprising the steps of:

(a) removing a sample of spinal cord tissue from a rodent or human embryo at a stage of embryonic development after closure of the neural tube but prior to differentiation of glial and neuronal cells in the neural tube;

(b) dissociating cells comprising the sample of spinal cord tissue removed from the embryo;

(c) purifying from the dissociated cells via an embryonic neural cell adhesion molecule antibody a subpopulation expressing embryonic neural cell adhesion molecule;

(d) plating the purified subpopulation of cells in feeder-cell-independent culture on a substratum and in a medium configured for supporting adherent growth of the neuron-restricted precursor cells; and

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(e) incubating the plated cells at a temperature and in an atmosphere conducive to growth to obtain an isolated, pure population of neuron-restricted precursor cells, wherein said neuron-restricted precursor cells require FGF for adherent growth, differentiate into CNS neuronal cells upon replacement of adherent growth supporting medium with retinoic acid containing medium and fail to proliferate or differentiate in astrocyte-promoting medium containing FGF and 10% fetal calf serum.

28. (amended) A method of producing rodent or human postmitotic neurons from rodent or human neuron-restricted precursor cells comprising:

(a) culturing rodent or human neuron-restricted precursor cells which require FGF and differentiate into CNS neuronal cells but not into CNS glial cells in proliferating conditions; and

(b) changing the culture conditions of the rodent or human neuron-restricted precursor cells from proliferating conditions to differentiating conditions, thereby causing the neuron-restricted precursor cells to differentiate into postmitotic neurons.

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59. (amended) A method of isolating a pure population of mouse or human CNS neuron-restricted precursor cells comprising the steps of:

- (a) providing a sample of mouse or human embryonic stem cells;
- (b) purifying from the mouse or human embryonic stem cells via an embryonic neural cell adhesion molecule antibody a subpopulation expressing embryonic neural cell adhesion molecule;
- (c) plating the purified subpopulation of cells in feeder-cell-independent culture on a substratum and in a medium configured for supporting adherent growth of the neuron-restricted precursor cells; and
- (d) incubating the plated cells at a temperature and in an atmosphere conducive to growth of the neuron-restricted precursor cells, wherein said neuron-restricted precursor cells require FGF and differentiate into CNS neuronal cells but not into CNS glial cells.